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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 02/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/650,595	CHEN ET AL.	
	Examiner	Art Unit	
	Stacy B Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *13-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/19/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. In the response filed November 19, 2004, Applicant's election with traverse of Group I, claims 1-12 is acknowledged. Applicant argues that because the claimed antigen-detection method of Group II relies on the multiconstituent calibrator of Group I, they cannot be separated from each other when the claimed method is practiced. Applicant also argues that there is no additional, unreasonable burden on the examiner to examine both groups together. In response, the Office has carefully considered Applicant's arguments but does not consider them to be persuasive. While the composition of Group I is capable of being used in the method of Group II, the composition is useable in another materially different method of use, as outlined previously. A literature search for a composition of heterologous antibodies will not necessarily reveal references directed to the method of Group II. It would be a serious burden to examine both groups of inventions. Therefore, the restriction requirement is deemed proper and made FINAL. Claims 1-12 are under examination. Claims 13-25 are withdrawn from consideration, being drawn to non-elected inventions.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 6-12 recite the limitation, "wherein said different antigens are derived from one or more organisms". Claim 7 recites the limitation, "wherein said different antigens

derived from Epstein-Barr (EBV) comprise antigens derived from" etc. The term "derived" is unclear and does not clearly define the metes and bounds of the structure of the antigen. "Derived" implies that something was taken from an original source. The process of deriving something from a source often includes changes to the derived product. In this instance, the antigen is taken from an organism or another antigen, but it is unclear what remains of the antigen after the derivation process. In other words, it is not clear what the antigen retains from the original source. If Applicant intends the term "derived" to simply mean that the antigen is from an organism or from an antigen, then it is suggested that the claims be amended to remove "derived".

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Guilbert *et al.* (*J. Immunology*, 1982, 128(6):2779-2787, herein, "Guilbert"). The claims are drawn to a composition comprising serum in which are dissolved a plurality of heterologous antibodies that are independently IgG or IgM, each of said antibodies specifically binding to different antigens. Specifically, the composition comprises three or five heterologous antibodies.

Guilbert discloses naturally occurring antibodies against nine common antigens in human sera. A composition comprising a serum pool from 800 human donors and individual sera from

three individual donors was passed through columns having immunoadsorbents of nine different antigens (abstract). IgG, IgA and IgM antibodies were detected against tubulin, actin, tyroglobulin, myoglobin, fetuin, transferrin, albumin, cytochrome c, and collagen (see Table 2). Antibodies that bind to different antigens are heterologous relative to each other. Guilbert teaches that antibodies from the human sera were not as specific for their respective antigens as are induced antibodies, however, the antibodies were still deemed to be specific (page 2779, second column, third full paragraph). Since the claims broadly encompass antibodies to any antigens with any specificity, the claims are anticipated by Guilbert.

4. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Berneman *et al.* (*Eur. J. Immunol.* 1992, 22 :625-633, herein, "Berneman"). The claims are drawn to a composition comprising serum in which are dissolved a plurality of heterologous antibodies that are independently IgG or IgM, each of said antibodies specifically binding to different antigens. Specifically, the composition comprises three, five, ten or fifteen heterologous antibodies.

Berneman discloses mouse sera containing IgG to mouse self antigens. Berneman separated IgG and IgM from serum and found that both were reactive with numerous (exceeding fifteen) antigens in Tables 1 and 2. Berneman discovered that antibody reactivity was greater when IgG and IgM were separated from serum. Nevertheless, Berneman's IgG and IgM came from serum that originally contained the IgG and IgM antibodies. Therefore, Berneman's composition was comprised of at least fifteen heterologous antibodies to mouse self-antigens. Since the claims broadly encompass antibodies to any antigens with any specificity, the claims are anticipated by Berneman.

5. Claims 1-3 and 6-8 rejected under 35 U.S.C. 102(b) as being anticipated by Luka *et al.* (*J. Immunological Methods*, 1984, 67:145-156, herein, "Luka"). The claims are drawn to a composition comprising serum in which are dissolved a plurality of heterologous antibodies that are independently IgG or IgM, each of said antibodies specifically binding to different antigens. Specifically, the composition comprises heterologous antibodies from Epstein-Barr virus: capsid antigen (VCA), nuclear antigen type 1 (NA1) and early antigen diffused (EAD).

Luka discloses an ELISA method for detecting the major EBV-associated antigens. Luka discloses that the major antigens are VCA, nuclear antigen (also called nuclear antigen type 1 because it was the first EBV nuclear antigen discovered), membrane antigen and early antigen (abstract). Early antigen is a complex which comprises diffuse (EAD) and restricted (EAR) components (page 145, first paragraph). Luka prepared EBV antigens from monoclonal antibodies directed to EAD, EAR, VCA and membrane antigen (page 148, first paragraph). Luka's nuclear antigen was purified from Raji cells. In order to determine the optimal antigen concentrations to use in the ELISA assay for each of the EBV proteins, microplates were coated with varying antigen dilutions and then screened with sera. One of the serum pools used for the screening contained antibodies to nuclear antigen, VCA, EA and membrane antigen. Although Luka does not specifically say that the serum pool contained antibodies to EAD, one would expect EAD antibodies to be present because Luka prepared EAD antigen for the ELISA (page 148, first paragraph). Therefore, Luka anticipates the claims because Luka's composition contains serum and heterologous antibodies to the EBV major antigens.

6. Claims 1 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Wong *et al.* (US Patent 5,478,753, herein, "Wong"). The claims are drawn to a composition comprising serum in which are dissolved a plurality of heterologous antibodies that are independently IgG or IgM, each of said antibodies specifically binding to different antigens. Specifically, the antibodies bind to antigens from one or more organisms selected from the group of organisms in claim 6.

Wong discloses a calibrator/control composition for an IgM serology assay and an IgG serology assay. The composition comprises a composite antibody that has a non-specific IgM immunoglobulin moiety linked to a specific, non-IgM antibody moiety, such as IgG. Wong teaches that the composite antibodies are prepared in non-reactive human serum (col. 5, lines 4-12). IgG specific antibodies to *Toxoplasma*, rubella, cytomegalovirus (CMV) and herpesvirus can be incorporated into the composite antibody. A plurality of antibodies can be used in one assay (col. 5, lines 15-25). Therefore, Wong anticipates claim 1 and 6 by teaching a calibrator composition comprising serum and a plurality of antibodies specific for antigens.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wong in view of Desmonts *et al.* (US Patent 4,612,281, herein, "Desmonts"). Claim 10 is drawn to a composition

comprising serum in which are dissolved a plurality of heterologous antibodies that are independently IgG or IgM, each of said antibodies specifically binding to different antigens. Specifically, the antibodies bind to antigens from *Toxoplasma gondii*, Rubella virus, Cytomegalovirus (CMV), and Herpes Simplex Virus types 1 and 2 (HSV-1, HSV-2). Wong discloses a calibrator/control composition for an IgM serology assay and an IgG serology assay. The composition comprises a composite antibody that has a non-specific IgM immunoglobulin moiety linked to a specific, non-IgM antibody moiety, such as IgG. Wong teaches that the composite antibodies are prepared in non-reactive human serum (col. 5, lines 4-12). IgG specific antibodies to *Toxoplasma*, rubella, CMV, HSV-1 and HSV-2 can be incorporated into the composite antibody (col. 2, lines 37-44). A plurality of antibodies can be used in one assay (col. 5, lines 15-25). Wong is silent on the inclusion of IgM and IgG to *T. gondii*.

However, Desmonts discloses an assay for detecting IgG and IgM antibodies against *T. gondii* (abstract). It would have been obvious to include antibodies to *T. gondii* in Wong's calibrator composition because Wong suggests the use of antibodies to *Toxoplasma* generally (col. 5, lines 15-25). One would have been motivated to include other antibodies because Wong suggests the use a plurality of antibodies in one calibrator composition, such as antibodies to any infectious disease (claims 1 and 7, col. 2, lines 37-44 and col. 5, lines 15-25). One would have had a reasonable expectation of success that antibodies to *T. gondii* would have worked in the composition of Wong because Desmonts discloses that the antibodies detect *T. gondii*. Therefore, claim 10 is obvious over Wong in view of Desmonts.

8. Claims 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong in view of Desmonts as applied to claim 10 above, and further in view of Gans *et al.* (*J. Infect. Dis.*, 2001, 184:817-826, herein, "Gans"), Yi *et al.* (US Patent 6,794,153, herein, "Yi"), Krell *et al.* (US Patent 6,479,248, herein, "Krell") and Luka. The claims are drawn to a composition comprising serum in which are dissolved a plurality of heterologous antibodies that are independently IgG or IgM, each of said antibodies specifically binding to different antigens. Specifically, the composition comprises heterologous antibodies that bind to Epstein-Barr virus: capsid antigen (VCA), nuclear antigen type 1 (NA1) and early antigen diffused (EAD). In another embodiment, the antibodies bind to antigens from *T. gondii*, Rubella virus, CMV, HSV-1, HSV-2, Mumps, Measles, Varicella Zoster (VZV), *Treponema pallidum*, *Helicobacter pylori*, EBV-VCA, EBV-NA1 and EBV-EAD.

The teachings of Wong and Desmonts are summarized above. Wong also teaches antibodies to VZV in the calibrator composition (col. 2, lines 37-44). Wong is silent on the use of antibodies that specifically bind mumps, measles, *T. pallidum*, *H. pylori* and EBV-VCA, EBV-NA1 and EBV-EAD. However, Gans discloses immune responses in infants to the MMR (measles, mumps, rubella) vaccine (abstract). Yi discloses detection of *H. pylori* and its antibodies (abstract). Krell discloses detecting antibodies to *T. pallidum.* Luka discloses an ELISA method for detecting the major EBV-associated antigens and a serum panel using antibodies against VCA, NA and EAD (see the teachings of Luka summarized above). It would have been obvious to include the antibodies of Gans, Yi, Krell and Luka in Wong's calibrator composition. One would have been motivated to include other antibodies because Wong suggests the use a plurality of antibodies in one calibrator composition, such as antibodies to any

infectious disease (claims 1 and 7, col. 2, lines 37-44 and col. 5, lines 15-25). One would have had a reasonable expectation of success that the antibodies to mumps, measles, *T. Pallidum*, *H. pylori* and EBV-VCA, EBV-NA1 and EBV-EAD would have worked in the composition of Wong and Desmonts because those antibodies bind antigens of mumps, measles, *T. Pallidum*, *H. pylori* and EBV-VCA, EBV-NA1 and EBV-EAD. Therefore, the claims are obvious over Wong in view of Desmonts as applied to claim 10 above, and further in view of Gans, Yi, Krell and Luka.

9. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wong in view of Desmonts, Gans, Yi, Krell and Luka as applied to claims 9 and 11 above, and further in view of Lo *et al.* (US Patent 5,532,134, herein, "Lo"). The claims are drawn to a composition comprising serum in which are dissolved a plurality of heterologous antibodies that are independently IgG or IgM, each of said antibodies specifically binding to different antigens. Specifically, the antibodies bind to antigens from *T. gondii*, Rubella virus, CMV, HSV-1, HSV-2, Mumps, Measles, Varicella Zoster (VZV), *Borrelia burgdorferi*, *Treponema pallidum*, *Helicobacter pylori*, *Mycoplasma pneumoniae*, EBV-VCA, EBV-NA1 and EBV-EAD.

The teachings of Wong, Desmonts, Gans, Yi, Krell and Luka are summarized above. Additionally, Wong discloses the use of antibodies to the infectious agent of lyme disease, which is *Borrelia burgdorferi*. The combined teachings of the above mentioned references do not teach the use of antibodies to *Mycoplasma pneumoniae*. However, Lo discloses an assay for detecting *M. pneumoniae* and its antibodies (abstract and Example 7). It would have been obvious to incorporate the antibody of Lo into the calibration composition of Wong. One would

have been motivated to use Lo's antibody because Wong suggests the use of a plurality of antibodies in one calibrator composition, such as antibodies to any infectious disease (claims 1 and 7, col. 2, lines 37-44 and col. 5, lines 15-25). One would have had a reasonable expectation of success that an antibody to *M. pneumoniae* would have worked in Wong's calibrator composition because the antibody binds to an antigen of *M. pneumoniae*. Therefore, the claims are obvious over Wong in view of Desmonts, Gans, Yi, Krell and Luka as applied to claims 9 and 11 above, and further in view of Lo.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

11. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Stacy B. Chen
January 28, 2005